


CLAIMS

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1. In a method which calls for administration of IFN- α , the improvement comprising co-administering an effective amount of an isolated immunostimulatory nucleic acid.
2. The improvement of claim 1, wherein the IFN- α is administered at a dose below the clinically established effective dose for IFN- α alone.
3. The improvement of claim 1, wherein the IFN- α is administered at the maximum tolerated dose for IFN- α in the absence of the nucleic acid.
4. The improvement of claim 1, wherein the IFN- α is administered at least 20 percent below the maximum tolerated dose of IFN- α in the subject.
5. The improvement of claim 1, wherein the IFN- α is administered at least 30 percent below the maximum tolerated dose of IFN- α in the subject.
6. The improvement of claim 1, wherein the IFN- α is administered at least 40 percent below the maximum tolerated dose of IFN- α in the subject.
7. The improvement of claim 1, wherein the IFN- α is administered at least 50 percent below the maximum tolerated dose of IFN- α in the subject.
8. The improvement of claim 1, wherein the immunostimulatory nucleic acid is modified.
9. The improvement of claim 1, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

10. The improvement of claim 1, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

11. The improvement of claim 1, wherein the immunostimulatory nucleic acid is not a
5 palindrome.

12. The improvement of claim 1, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

10 13. The improvement of claim 1, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

14. The improvement of claim 13, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.

15 15. The improvement of claim 13, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

16. The improvement of claim 1, wherein the immunostimulatory nucleic acid is any
20 combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

17. The improvement of claim 1, wherein the immunostimulatory nucleic acid is between
25 8 and 100 nucleotides in length.

18. The improvement of claim 1, wherein the immunostimulatory nucleic acid is between
12 and 40 nucleotides in length.

19. The improvement of claim 1, wherein the immunostimulatory nucleic acid has a
30 sequence selected from the group consisting of

ggGGTCAACGTTGAgggggG
tcgtcgttttgcgttttgcgtt
ggggtcgtcgttttgggggg

ODN 1585 SEQ ID NO:1
ODN 2022 SEQ ID NO:2
ODN 2184 SEQ ID NO:3

002260" 92727960

Sub
32
30

tcgtcgttttgtcgttttgggggg
ggggtcgacgtcgagggggg
ggggtcacgatgagggggg
ggGGGACGATCGTCggggggG
5 gggggtcgtacgacgggggg
ggGGGACGATATCGTCggggggG
ggGGGACGACGTCGTCggggggG
ggGGGACGAGCTCGTCggggggG
ggGGGACGTACGTCggggggG
10 ggGGGACGATCGTTGgggggG
ggGGAACGATCGTCggggggG
ggGGGGACGATCGTCggggggG
ggGGGACGATCGTCGggggggG
ggGGGTCATCGATGAggggggG
15 ggGGTCGTCGACGAggggggG
ggGGTCGTTTGAACGAggggggG
ggGGACGTTTGAACGTggggggG
ggGGAACGACGTCGTTggggggG
ggGGAACGTACGTCggggggG
20 ggGGAACGTACGTACGTTggggggG
ggGGTCACCGGTGAggggggG
ggGGTCGACGTACGTGAggggggG
ggGGACCGGTACCGGTggggggG
ggGTCGACGTCGAggggggG
25 ggGGTCGACGTCGagggg
ggGGAACGTTAACGTTggggggG
ggGGACGTCGACGTgggggG
ggGGGTCGTTTCGTTggggggG
ggGACGATCGTCGggggggG
30 ggGTCGTCGACGAggggggG
ggTCGTCGACGAGggggggG
ggGGACGATCGTCGggggggG
ggGGTCGACGTCGACGTCGAGggggggG
ggGGACGACGTCGTGggggggG

ODN 2185 SEQ ID NO:4
ODN 2192 SEQ ID NO:5
ODN 2204 SEQ ID NO:6
ODN 2216 SEQ ID NO:7
ODN 2217 SEQ ID NO:8
ODN 2245 SEQ ID NO:9
ODN 2246 SEQ ID NO:10
ODN 2247 SEQ ID NO:11
ODN 2248 SEQ ID NO:12
ODN 2252 SEQ ID NO:13
ODN 2253 SEQ ID NO:14
ODN 2254 SEQ ID NO:15
ODN 2255 SEQ ID NO:16
ODN 2260 SEQ ID NO:17
ODN 2293 SEQ ID NO:18
ODN 2294 SEQ ID NO:19
ODN 2295 SEQ ID NO:20
ODN 2297 SEQ ID NO:21
ODN 2298 SEQ ID NO:22
ODN 2299 SEQ ID NO:23
ODN 2300 SEQ ID NO:24
ODN 2301 SEQ ID NO:25
ODN 2302 SEQ ID NO:26
ODN 2303 SEQ ID NO:27
ODN 2304 SEQ ID NO:28
ODN 2305 SEQ ID NO:29
ODN 2306 SEQ ID NO:30
ODN 2311 SEQ ID NO:31
ODN 2328 SEQ ID NO:32
ODN 2329 SEQ ID NO:33
ODN 2330 SEQ ID NO:34
ODN 2332 SEQ ID NO:35
ODN 2334 SEQ ID NO:36, and
ODN 2336 SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

20. The improvement of claim 1, further comprising co-administering GM-CSF to the subject.

21. The improvement of claim 1, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

22. The improvement of claim 1, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

23. The improvement of claim 1, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

24. A method of supplementing IFN- α treatment of a subject comprising administering to a subject in need of IFN- α treatment an effective amount of IFN- α and an isolated immunostimulatory nucleic acid.

25. The method of claim 24, wherein the IFN- α is administered at a dose below the clinically established effective dose for IFN- α alone.

26. The method of claim 24, wherein the IFN- α is administered at the maximum tolerated dose for IFN- α in the absence of the immunostimulatory nucleic acid.

27. The method of claim 24, wherein the IFN- α is administered at least 20 percent below the maximum tolerated dose of IFN- α in the subject.

28. The method of claim 24, wherein the IFN- α is administered at least 30 percent below the maximum tolerated dose of IFN- α in the subject.

29. The method of claim 24, wherein the IFN- α is administered at least 40 percent below the maximum tolerated dose of IFN- α in the subject.

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30. The method of claim 24, wherein the IFN- α is administered at least 50 percent below the maximum tolerated dose of IFN- α in the subject.
31. The method of claim 24, wherein the immunostimulatory nucleic acid is modified.
32. The method of claim 24, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.
33. The method of claim 24, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.
34. The method of claim 24, wherein the immunostimulatory nucleic acid is not a palindrome.
35. The method of claim 24, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.
36. The method of claim 24, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.
37. The method of claim 36, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.
38. The method of claim 36, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.
39. The method of claim 24, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

40. The method of claim 24, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

41. The method of claim 24, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

42. The method of claim 24, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

10	ggGGTCAACGTTGAgggggG	ODN 1585	SEQ ID NO:1
	tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
	ggggtcgtcgttttggggg	ODN 2184	SEQ ID NO:3
	tcgtcgttttgcgttttggggg	ODN 2185	SEQ ID NO:4
	ggggtcgacgtcgaggggg	ODN 2192	SEQ ID NO:5
	ggggtcacgtcgaggggg	ODN 2204	SEQ ID NO:6
15	ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
	gggggtcgtacgacggggg	ODN 2217	SEQ ID NO:8
	ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
	ggGGGACGACGTCGTCgggggG	ODN 2246	SEQ ID NO:10
	ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
20	ggGGGACGTACGTCgggggG	ODN 2248	SEQ ID NO:12
	ggGGGACGATCGTTGggggG	ODN 2252	SEQ ID NO:13
	ggGGAACGATCGTCgggggG	ODN 2253	SEQ ID NO:14
	ggGGGGACGATCGTCgggggG	ODN 2254	SEQ ID NO:15
	ggGGGACGATCGTCGgggggG	ODN 2255	SEQ ID NO:16
25	ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17
	ggGGTCGTCGACGAgggggG	ODN 2293	SEQ ID NO:18
	ggGGTCGTTTCAACGAgggggG	ODN 2294	SEQ ID NO:19
	ggGGACGTTTCAACGTgggggG	ODN 2295	SEQ ID NO:20
	ggGGAACGACGTCGTTgggggG	ODN 2297	SEQ ID NO:21
30	ggGGAACGTACGTCgggggG	ODN 2298	SEQ ID NO:22
	ggGGAACGTACGTACGTTgggggG	ODN 2299	SEQ ID NO:23
	ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
	ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
	ggGGACCGGTACCGGTgggggG	ODN 2302	SEQ ID NO:26
35	ggGTCGACGTCGAgggggG	ODN 2303	SEQ ID NO:27
	ggGGTCGACGTCGagggg	ODN 2304	SEQ ID NO:28
	ggGGAACGTTAACGTTgggggG	ODN 2305	SEQ ID NO:29
	ggGGACGTCGACGTgggggG	ODN 2306	SEQ ID NO:30
	ggGGGTCGTTTCGTTgggggG	ODN 2311	SEQ ID NO:31
40	ggGACGATCGTCGgggggG	ODN 2328	SEQ ID NO:32
	ggGTCGTCGACGAggggggG	ODN 2329	SEQ ID NO:33
	ggTCGTCGACGAGgggggG	ODN 2330	SEQ ID NO:34
	ggGGACGATCGTCGgggggG	ODN 2332	SEQ ID NO:35
	ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and

ggGGACGACGTCGTGgggggG

ODN 2336 SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

43. The method of claim 24, further comprising co-administering GM-CSF to the subject.

44. The method of claim 24, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

45. The method of claim 24, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

46. The method of claim 24, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

47. A method of treating a subject to activate interferon-producing cells (IPCs) of the subject comprising
isolating IPCs from a subject in need of such treatment,
culturing the IPCs *in vitro*,
contacting the IPCs *in vitro* with an effective amount of an isolated immunostimulatory nucleic acid, and
returning the contacted IPCs to the subject.

48. The method of claim 47, further comprising contacting the IPCs *in vitro* with a growth factor.

49. The method of claim 47, further comprising contacting the IPCs *in vitro* with IL-3.

50. The method of claim 47, further comprising contacting the IPCs *in vitro* with GM-CSF.
51. The method of claim 47, wherein the IPCs are cultured *in vitro* in the absence of IL-3.
52. The method of claim 47, wherein the IPCs are cultured *in vitro* in the absence of GM-CSF.
53. The method of claim 47, wherein the immunostimulatory nucleic acid is modified.
54. The method of claim 47, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.
55. The method of claim 47, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.
56. The method of claim 47, wherein the immunostimulatory nucleic acid is not a palindrome.
57. The method of claim 47, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.
58. The method of claim 47, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.
59. The method of claim 58, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.
60. The method of claim 58, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

61. The method of claim 47, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

62. The method of claim 47, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

63. The method of claim 47, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

64. The method of claim 47, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGTCAACGTTGAgggggG

tcgtcgtttgcgttttgcgtt

ggggtcgctgtttggggg

tcgtcgtttgcgttttggggg

ggggtcgacgtcgagggggg

ggggtcatcgatgagggggg

ggGGGACGATCGTCgggggG

gggggtcgtagcagggggg

ggGGGACGATATCGTCgggggG

ggGGGACGACGTCGTCgggggG

ggGGGACGAGCTCGTCgggggG

ggGGGACGTACGTCgggggG

ggGGGACGATCGTTGgggggG

ggGGAACGATCGTCgggggG

ggGGGACGATCGTCgggggG

ggGGGACGATCGTCgggggG

ggGGGTCATCGATGAgggggG

ggGGTCGTCGACGAgggggG

ggGGTCGTTTGAACGAgggggG

ggGGACGTTTGAACGTgggggG

ggGGAACGACGTCGTTgggggG

ggGGAACGTACGTCgggggG

ggGGAACGTACGTACGTTgggggG

ggGGTCACCGGTGAgggggG

ggGGTCGACGTACGTCGAgggggG

ggGGACCGGTACCGGTgggggG

ggGTCGACGTCGAgggggG

ggGGTCGACGTCGAgggg

ggGGAACGTTAACGTTgggggG

ODN 1585 SEQ ID NO:1

ODN 2022 SEQ ID NO:2

ODN 2184 SEQ ID NO:3

ODN 2185 SEQ ID NO:4

ODN 2192 SEQ ID NO:5

ODN 2204 SEQ ID NO:6

ODN 2216 SEQ ID NO:7

ODN 2217 SEQ ID NO:8

ODN 2245 SEQ ID NO:9

ODN 2246 SEQ ID NO:10

ODN 2247 SEQ ID NO:11

ODN 2248 SEQ ID NO:12

ODN 2252 SEQ ID NO:13

ODN 2253 SEQ ID NO:14

ODN 2254 SEQ ID NO:15

ODN 2255 SEQ ID NO:16

ODN 2260 SEQ ID NO:17

ODN 2293 SEQ ID NO:18

ODN 2294 SEQ ID NO:19

ODN 2295 SEQ ID NO:20

ODN 2297 SEQ ID NO:21

ODN 2298 SEQ ID NO:22

ODN 2299 SEQ ID NO:23

ODN 2300 SEQ ID NO:24

ODN 2301 SEQ ID NO:25

ODN 2302 SEQ ID NO:26

ODN 2303 SEQ ID NO:27

ODN 2304 SEQ ID NO:28

ODN 2305 SEQ ID NO:29

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ggGGACGTCGACGTgggggG	ODN 2306	SEQ ID NO:30
ggGGGTCGTTCGTTgggggG	ODN 2311	SEQ ID NO:31
ggGACGATCGTCGgggggG	ODN 2328	SEQ ID NO:32
ggGTCGTCGACGAGgggggG	ODN 2329	SEQ ID NO:33
5 ggTCGTCGACGAGgggggG	ODN 2330	SEQ ID NO:34
ggGGACGATCGTCGgggggG	ODN 2332	SEQ ID NO:35
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

65. A method of increasing efficacy of IFN- α treatment of a subject, comprising:
administering to a subject in need of treatment with IFN- α a pharmaceutical composition comprising IFN- α , and
15 coadministering to the subject in need of such treatment a pharmaceutical composition comprising an immunostimulatory nucleic acid in an amount which, together with the administered IFN- α , is an effective IFN- α treatment, wherein the efficacy of the IFN- α treatment is greater than the efficacy of administering the same amount of IFN- α in the absence of coadministering the immunostimulatory nucleic acid.
- 20 66. The method of claim 65, wherein the pharmaceutical composition comprising an immunostimulatory nucleic acid is administered locally.
- 25 67. The method of claim 65, wherein the immunostimulatory nucleic acid is modified.
68. The method of claim 65, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.
- 30 69. The method of claim 65, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

70. The method of claim 65, wherein the immunostimulatory nucleic acid is not a palindrome.

71. The method of claim 65, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

72. The method of claim 65, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

73. The method of claim 72, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.

74. The method of claim 72, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

75. The method of claim 65, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

76. The method of claim 65, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

77. The method of claim 65, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

78. The method of claim 65, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGTCAACGTTGAgggggG
tcgtcgtttgtcgtttgtcgtt
ggggtcgtcgtttgggggg
tcgtcgtttgtcgtttgggggg
ggggtcgacgtcgagggggg
ggggtcacgtcgagggggg
ggGGGACGATCGTCgggggG
gggggtcgtacgagggggg

ODN 1585	SEQ ID NO:1
ODN 2022	SEQ ID NO:2
ODN 2184	SEQ ID NO:3
ODN 2185	SEQ ID NO:4
ODN 2192	SEQ ID NO:5
ODN 2204	SEQ ID NO:6
ODN 2216	SEQ ID NO:7
ODN 2217	SEQ ID NO:8

ggGGGACGATATCGTCggggggG
 ggGGGACGACGTCGTCggggggG
 ggGGGACGAGCTCGTCggggggG
 ggGGGACGTACGTCggggggG
 5 ggGGGACGATCGTTGgggggG
 ggGGAACGATCGTCggggggG
 ggGGGGACGATCGTCggggggG
 ggGGGACGATCGTCGggggggG
 ggGGGTCATCGATGAggggggG
 10 ggGGTCGTCGACGAggggggG
 ggGGTCGTTCTGAACGAggggggG
 ggGGACGTTCTGAACGTggggggG
 ggGGAACGACGTCGTTggggggG
 ggGGAACGTACGTCggggggG
 15 ggGGAACGTACGTACGTTggggggG
 ggGGTCACCGGTGAggggggG
 ggGGTCGACGTACGTCGAggggggG
 ggGGACCGGTACCGGTggggggG
 ggGTCGACGTCGAggggggG
 20 ggGGTCGACGTCGAggggg
 ggGGAACGTTAACGTTggggggG
 ggGGACGTCGACGTgggggG
 ggGGGTCGTTCTGTTggggggG
 ggGACGATCGTCGggggggG
 25 ggGTCGTCGACGAgggggggG
 ggTCGTCGACGAGggggggG
 ggGGACGATCGTCGggggggG
 ggGGTCGACGTCGACGTCGAGggggggG
 ggGGACGACGTCGTGggggggG

ODN 2245 SEQ ID NO:9
 ODN 2246 SEQ ID NO:10
 ODN 2247 SEQ ID NO:11
 ODN 2248 SEQ ID NO:12
 ODN 2252 SEQ ID NO:13
 ODN 2253 SEQ ID NO:14
 ODN 2254 SEQ ID NO:15
 ODN 2255 SEQ ID NO:16
 ODN 2260 SEQ ID NO:17
 ODN 2293 SEQ ID NO:18
 ODN 2294 SEQ ID NO:19
 ODN 2295 SEQ ID NO:20
 ODN 2297 SEQ ID NO:21
 ODN 2298 SEQ ID NO:22
 ODN 2299 SEQ ID NO:23
 ODN 2300 SEQ ID NO:24
 ODN 2301 SEQ ID NO:25
 ODN 2302 SEQ ID NO:26
 ODN 2303 SEQ ID NO:27
 ODN 2304 SEQ ID NO:28
 ODN 2305 SEQ ID NO:29
 ODN 2306 SEQ ID NO:30
 ODN 2311 SEQ ID NO:31
 ODN 2328 SEQ ID NO:32
 ODN 2329 SEQ ID NO:33
 ODN 2330 SEQ ID NO:34
 ODN 2332 SEQ ID NO:35
 ODN 2334 SEQ ID NO:36, and
 ODN 2336 SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

79. The method of claim 65, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

80. The method of claim 65, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

81. The method of claim 65, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

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82. A method of decreasing a dose of IFN- α effective for treating a subject, comprising:
administering to a subject in need of treatment with IFN- α a pharmaceutical composition comprising IFN- α , and
coadministering to the subject in need of such treatment a pharmaceutical composition comprising an immunostimulatory nucleic acid in an amount which, together
10 with the administered IFN- α , is an effective IFN- α treatment, and, wherein the amount of administered IFN- α is less than an amount of IFN- α required in the absence of coadministering the immunostimulatory nucleic acid.

15 83. The method of claim 82, wherein the amount of administered IFN- α is at least 20 percent below the amount of IFN- α required in the absence of coadministering the immunostimulatory nucleic acid.

20 84. The method of claim 82, wherein the amount of administered IFN- α is at least 30 percent below the amount of IFN- α required in the absence of coadministering the immunostimulatory nucleic acid.

25 85. The method of claim 82, wherein the amount of administered IFN- α is at least 40 percent below the amount of IFN- α required in the absence of coadministering the immunostimulatory nucleic acid.

30 86. The method of claim 82, wherein the amount of administered IFN- α is at least 50 percent below the amount of IFN- α required in the absence of coadministering the immunostimulatory nucleic acid.

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87. The method of claim 82, wherein the pharmaceutical composition comprising an immunostimulatory nucleic acid is administered locally.
88. The method of claim 82, wherein the immunostimulatory nucleic acid is modified.
89. The method of claim 82, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.
90. The method of claim 82, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.
91. The method of claim 82, wherein the immunostimulatory nucleic acid is not a palindrome.
92. The method of claim 82, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.
93. The method of claim 82, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.
94. The method of claim 93, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.
95. The method of claim 93, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.
96. The method of claim 82, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

97. The method of claim 82, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

98. The method of claim 82, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

99. The method of claim 82, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGTCAACGTTGAggggggG	ODN 1585	SEQ ID NO:1
tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
ggggtcgtcgttttgggggg	ODN 2184	SEQ ID NO:3
tcgtcgttttgcgttttgggggg	ODN 2185	SEQ ID NO:4
ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
ggggtcacgtcgagggggg	ODN 2204	SEQ ID NO:6
ggGGGACGATCGTCggggggG	ODN 2216	SEQ ID NO:7
gggggtcgtagcagggggg	ODN 2217	SEQ ID NO:8
ggGGGACGATATCGTCggggggG	ODN 2245	SEQ ID NO:9
ggGGGACGACGTCGTCggggggG	ODN 2246	SEQ ID NO:10
ggGGGACGAGCTCGTCggggggG	ODN 2247	SEQ ID NO:11
ggGGGACGTACGTCggggggG	ODN 2248	SEQ ID NO:12
ggGGGACGATCGTTggggggG	ODN 2252	SEQ ID NO:13
ggGGAACGATCGTCggggggG	ODN 2253	SEQ ID NO:14
ggGGGACGATCGTCggggggG	ODN 2254	SEQ ID NO:15
ggGGGACGATCGTCGggggggG	ODN 2255	SEQ ID NO:16
ggGGGTCATCGATGAggggggG	ODN 2260	SEQ ID NO:17
ggGGTCGTCGACGAggggggG	ODN 2293	SEQ ID NO:18
ggGGTCGTTTCAACGAggggggG	ODN 2294	SEQ ID NO:19
ggGGACGTTTCAACGTggggggG	ODN 2295	SEQ ID NO:20
ggGGAACGACGTCGTTggggggG	ODN 2297	SEQ ID NO:21
ggGGAACGTACGTCggggggG	ODN 2298	SEQ ID NO:22
ggGGAACGTACGTACGTTggggggG	ODN 2299	SEQ ID NO:23
ggGGTCACCGGTGAggggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAggggggG	ODN 2301	SEQ ID NO:25
ggGGACCGGTACCGGTggggggG	ODN 2302	SEQ ID NO:26
ggGTCGACGTCGAggggggG	ODN 2303	SEQ ID NO:27
ggGGTCGACGTCGagggg	ODN 2304	SEQ ID NO:28
ggGGAACGTTAACGTTggggggG	ODN 2305	SEQ ID NO:29
ggGGACGTCGACGTggggggG	ODN 2306	SEQ ID NO:30
ggGGGTCGTTTCGTTggggggG	ODN 2311	SEQ ID NO:31
ggGACGATCGTCGggggggG	ODN 2328	SEQ ID NO:32
ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
ggTCGTCGACGAGggggggG	ODN 2330	SEQ ID NO:34
ggGGACGATCGTCGggggggG	ODN 2332	SEQ ID NO:35
ggGGTCGACGTCGACGTCGAGggggggG	ODN 2334	SEQ ID NO:36, and

ggGACGACGTCGTGgggggG

ODN 2336 SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

100. The method of claim 82, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

101. The method of claim 82, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

102. The method of claim 82, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

103. A method of preventing an IFN- α treatment-related side effect in a subject receiving or in need of treatment with IFN- α , comprising
administering to a subject in need of treatment with IFN- α a pharmaceutical composition comprising IFN- α , and
coadministering to the subject in need of such treatment a pharmaceutical composition comprising an immunostimulatory nucleic acid in an amount which, together with the administered IFN- α , is an effective IFN- α treatment, and, wherein an IFN- α treatment-related side effect is reduced in comparison to the side effect when IFN- α is administered in the absence of coadministering the immunostimulatory nucleic acid.

104. The method of claim 103, wherein the pharmaceutical composition comprising an immunostimulatory nucleic acid is administered locally.

105. The method of claim 103, wherein the IFN- α treatment-related side effect is systemic.

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106. The method of claim 103, wherein the IFN- α treatment-related side effect is selected from the group consisting of flu-like syndrome, fever, headache, chills, myalgia, fatigue, anorexia, nausea, vomiting, diarrhea, and depression.

5

107. The method of claim 103, wherein the immunostimulatory nucleic acid is modified.

108. The method of claim 103, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

10

109. The method of claim 103, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

15

110. The method of claim 103, wherein the immunostimulatory nucleic acid is not a palindrome.

111. The method of claim 103, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

20

112. The method of claim 103, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

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113. The method of claim 112, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.

114. The method of claim 112, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

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115. The method of claim 103, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

116. The method of claim 103, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

117. The method of claim 103, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

118. The method of claim 103, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGTCAACGTTGAgggggG	ODN 1585	SEQ ID NO:1
tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
ggggtcgtcgttttggggggg	ODN 2184	SEQ ID NO:3
tcgtcgttttgcgttttggggggg	ODN 2185	SEQ ID NO:4
ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
ggggtcacgtcgagggggg	ODN 2204	SEQ ID NO:6
ggGGGACGATCGTCggggggG	ODN 2216	SEQ ID NO:7
gggggtcgtacgacgggggg	ODN 2217	SEQ ID NO:8
ggGGGACGATATCGTCggggggG	ODN 2245	SEQ ID NO:9
ggGGGACGACGTCGTCggggggG	ODN 2246	SEQ ID NO:10
ggGGGACGAGCTCGTCggggggG	ODN 2247	SEQ ID NO:11
ggGGGACGTACGTCggggggG	ODN 2248	SEQ ID NO:12
ggGGGACGATCGTTGggggggG	ODN 2252	SEQ ID NO:13
ggGGAACGATCGTCggggggG	ODN 2253	SEQ ID NO:14
ggGGGGACGATCGTCggggggG	ODN 2254	SEQ ID NO:15
ggGGGACGATCGTCGggggggG	ODN 2255	SEQ ID NO:16
ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17
ggGGTCGTCGACGAgggggG	ODN 2293	SEQ ID NO:18
ggGGTCGTTTCAACGAgggggG	ODN 2294	SEQ ID NO:19
ggGGACGTTTCAACGTggggggG	ODN 2295	SEQ ID NO:20
ggGGAACGACGTCGTTggggggG	ODN 2297	SEQ ID NO:21
ggGGAACGTACGTCggggggG	ODN 2298	SEQ ID NO:22
ggGGAACGTACGTACGTTggggggG	ODN 2299	SEQ ID NO:23
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACCGGTACCGGTggggggG	ODN 2302	SEQ ID NO:26
ggGTCGACGTCGAgggggG	ODN 2303	SEQ ID NO:27
ggGGTCGACGTCGAggggg	ODN 2304	SEQ ID NO:28
ggGGAACGTTAACGTTggggggG	ODN 2305	SEQ ID NO:29
ggGGACGTCGACGTgggggG	ODN 2306	SEQ ID NO:30

ggGGGTCGTTCGTTggggggG	ODN 2311	SEQ ID NO:31
ggGACGATCGTCGggggggG	ODN 2328	SEQ ID NO:32
ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
ggTCGTCGACGAGggggggG	ODN 2330	SEQ ID NO:34
5 ggGGACGATCGTCGggggggG	ODN 2332	SEQ ID NO:35
ggGGTTCGACGTCGACGTCGAGggggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGggggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

119. The method of claim 103, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

120. The method of claim 103, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

121. The method of claim 103, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

122. A method of enhancing efficacy of IFN- α treatment in a subject in need of such treatment, comprising

administering to a subject in need of such treatment an amount of a pharmaceutical composition comprising IFN- α effective for treating a condition of the subject;

isolating natural interferon-producing cells (IPCs) from a donor;

contacting the isolated IPCs *ex vivo* with an amount of a pharmaceutical composition comprising an immunostimulatory nucleic acid effective for inducing the IPCs to release IFN- α ; and

administering the contacted cells to the subject.

123. The method of claim 122, wherein the donor is the subject.

124. The method of claim 122 further comprising contacting the isolated IPCs with an
5 antigen.

125. The method of claim 122, wherein the administering the contacted cells comprises
local injection.

10 126. The method of claim 125, wherein the local injection is via a blood vessel supplying a
target tissue.

127. The method of claim 126, wherein the blood vessel is selected from the group
consisting of a hepatic artery, a portal vein, a celiac artery, and a splenic artery.

15 128. The method of claim 122, wherein the immunostimulatory nucleic acid is modified.

129. The method of claim 122, wherein the immunostimulatory nucleic acid comprises a
backbone with at least one nuclease-resistant internucleotide linkage selected from the
20 group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and
peptide.

130. The method of claim 122, wherein the immunostimulatory nucleic acid comprises at
least one nucleotide analog or derivative.

25 131. The method of claim 122, wherein the immunostimulatory nucleic acid is not a
palindrome.

132. The method of claim 122, wherein the immunostimulatory nucleic acid is a CpG
30 nucleic acid.

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133. The method of claim 122, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

134. The method of claim 133, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.

135. The method of claim 133, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

136. The method of claim 122, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

137. The method of claim 122, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

138. The method of claim 122, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

139. The method of claim 122, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGTCAACGTTGAgggggG	ODN 1585	SEQ ID NO:1
tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
ggggtcgtcgttttgggggg	ODN 2184	SEQ ID NO:3
tcgtcgttttgcgttttgggggg	ODN 2185	SEQ ID NO:4
ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
ggggtcacgtcgagggggg	ODN 2204	SEQ ID NO:6
ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
gggggtcgtacgacggggg	ODN 2217	SEQ ID NO:8
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGACGTCGTCgggggG	ODN 2246	SEQ ID NO:10
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGTACGTCgggggG	ODN 2248	SEQ ID NO:12
ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
ggGGAACGATCGTCgggggG	ODN 2253	SEQ ID NO:14
ggGGGACGATCGTCgggggG	ODN 2254	SEQ ID NO:15
ggGGGACGATCGTCGgggggG	ODN 2255	SEQ ID NO:16
ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17

	ggGGTCGTCGACGAggggggG	ODN 2293	SEQ ID NO:18
	ggGGTCGTTCTGAACGAggggggG	ODN 2294	SEQ ID NO:19
	ggGGACGTTCTGAACGTggggggG	ODN 2295	SEQ ID NO:20
	ggGGAACGACGTCGTTggggggG	ODN 2297	SEQ ID NO:21
5	ggGGAACGTACGTCggggggG	ODN 2298	SEQ ID NO:22
	ggGGAACGTACGTACGTTggggggG	ODN 2299	SEQ ID NO:23
	ggGGTCACCGGTGAggggggG	ODN 2300	SEQ ID NO:24
	ggGGTCGACGTACGTCGAggggggG	ODN 2301	SEQ ID NO:25
	ggGGACCGGTACCGGTggggggG	ODN 2302	SEQ ID NO:26
10	ggGTCGACGTCGAggggggG	ODN 2303	SEQ ID NO:27
	ggGGTCGACGTCGAgggggG	ODN 2304	SEQ ID NO:28
	ggGGAACGTTAACGTTggggggG	ODN 2305	SEQ ID NO:29
	ggGGACGTCGACGTggggggG	ODN 2306	SEQ ID NO:30
	ggGGGTCGTTCTGTTggggggG	ODN 2311	SEQ ID NO:31
15	ggGACGATCGTCGggggggG	ODN 2328	SEQ ID NO:32
	ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
	ggTCGTCGACGAGggggggG	ODN 2330	SEQ ID NO:34
	ggGGACGATCGTCGggggggG	ODN 2332	SEQ ID NO:35
	ggGGTCGACGTCGACGTCGAGggggggG	ODN 2334	SEQ ID NO:36, and
20	ggGGACGACGTCGTGggggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

140. The method of claim 122, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

141. The method of claim 122, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

142. The method of claim 122, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

143. A method of supporting survival of natural interferon-producing cells (IPCs) *in vitro*, comprising
isolating IPCs from a subject;
culturing the IPCs in a sterile medium suitable for tissue culture; and
5 contacting the IPCs *in vitro* with an amount of immunostimulatory nucleic acid effective to support the growth of the IPCs in the absence of interleukin 3 (IL-3).

144. The method of claim 143, wherein the IPCs are precursor type 2 dendritic cells (pDC2s).

145. The method of claim 143, wherein the IPCs are cultured in the absence of IL-3.

146. The method of claim 143, wherein the IPCs are cultured in the absence of GM-CSF.

147. The method of claim 143, wherein the immunostimulatory nucleic acid is modified.

148. The method of claim 143, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

149. The method of claim 143, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

150. The method of claim 143, wherein the immunostimulatory nucleic acid is not a palindrome.

151. The method of claim 143, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

152. The method of claim 143, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

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153. The method of claim 152, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.

5 154. The method of claim 152, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

155. The method of claim 143, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

156. The method of claim 143, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

15 157. The method of claim 143, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

158. The method of claim 143, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

20	ggGGTCAACGTTGAgggggG	ODN 1585	SEQ ID NO:1
	tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
	ggggtcgtcgttttgggggg	ODN 2184	SEQ ID NO:3
	tcgtcgttttgcgttttgggggg	ODN 2185	SEQ ID NO:4
	ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
25	ggggtcacgtcgagggggg	ODN 2204	SEQ ID NO:6
	ggGGGACGATCGTCggggggG	ODN 2216	SEQ ID NO:7
	gggggtcgtacgacgggggg	ODN 2217	SEQ ID NO:8
	ggGGGACGATATCGTCggggggG	ODN 2245	SEQ ID NO:9
	ggGGGACGACGTCGTCggggggG	ODN 2246	SEQ ID NO:10
30	ggGGGACGAGCTCGTCggggggG	ODN 2247	SEQ ID NO:11
	ggGGGACGTACGTCggggggG	ODN 2248	SEQ ID NO:12
	ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
	ggGGAACGATCGTCggggggG	ODN 2253	SEQ ID NO:14
	ggGGGACGATCGTCggggggG	ODN 2254	SEQ ID NO:15
35	ggGGGACGATCGTCGggggggG	ODN 2255	SEQ ID NO:16
	ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17
	ggGGTCGTCGACGAgggggG	ODN 2293	SEQ ID NO:18
	ggGGTCGTTTCAACGAgggggG	ODN 2294	SEQ ID NO:19
	ggGGACGTTTCAACGTggggggG	ODN 2295	SEQ ID NO:20

ggGGAACGACGTCGTTggggggG	ODN 2297	SEQ ID NO:21
ggGGAACGTACGTCggggggG	ODN 2298	SEQ ID NO:22
ggGGAACGTACGTACGTTggggggG	ODN 2299	SEQ ID NO:23
ggGGTCACCGGTGAggggggG	ODN 2300	SEQ ID NO:24
5 ggGGTCGACGTACGTCGAggggggG	ODN 2301	SEQ ID NO:25
ggGGACCGGTACCGGTggggggG	ODN 2302	SEQ ID NO:26
ggGTCGACGTCGAggggggG	ODN 2303	SEQ ID NO:27
ggGGTCGACGTCGagggg	ODN 2304	SEQ ID NO:28
ggGGAACGTTAACGTTggggggG	ODN 2305	SEQ ID NO:29
10 ggGGACGTCGACGTgggggG	ODN 2306	SEQ ID NO:30
ggGGGTCGTTTCGTTggggggG	ODN 2311	SEQ ID NO:31
ggGACGATCGTCGggggggG	ODN 2328	SEQ ID NO:32
ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
ggTCGTCGACGAGggggggG	ODN 2330	SEQ ID NO:34
15 ggGGACGATCGTCGggggggG	ODN 2332	SEQ ID NO:35
ggGGTCGACGTCGACGTCGAGggggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGggggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

159. A method of stimulating isolated interferon-producing cells (IPCs) *in vitro*, comprising

- isolating IPCs from a subject;
- culturing the IPCs in a sterile medium suitable for tissue culture; and
- 25 contacting the IPCs *in vitro* with an amount of immunostimulatory nucleic acid effective to induce secretion of at least one type I interferon.

160. The method of claim 159, wherein the IPCs are precursor type 2 dendritic cells (pDC2s).

161. The method of claim 159, wherein the type I interferon is an IFN- α .

162. The method of claim 159, wherein the IPCs are cultured in the absence of IL-3.

35 163. The method of claim 159, wherein the IPCs are cultured in the absence of GM-CSF.

164. The method of claim 159, wherein the immunostimulatory nucleic acid is modified.

165. The method of claim 159, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

166. The method of claim 159, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

167. The method of claim 159, wherein the immunostimulatory nucleic acid is not a palindrome.

168. The method of claim 159, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

169. The method of claim 159, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

170. The method of claim 169, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.

171. The method of claim 169, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

172. The method of claim 159, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

173. The method of claim 159, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

174. The method of claim 159, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

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175. The method of claim 159, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

	ggGGTCAACGTTGAgggggG	ODN 1585	SEQ ID NO:1
5	tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
	ggggtcgtcgttttgggggg	ODN 2184	SEQ ID NO:3
	tcgtcgttttgcgttttgggggg	ODN 2185	SEQ ID NO:4
	ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
	ggggtcacgtcgatgagggggg	ODN 2204	SEQ ID NO:6
10	ggGGGACGATCGTCggggggG	ODN 2216	SEQ ID NO:7
	gggggtcgtacgacgggggg	ODN 2217	SEQ ID NO:8
	ggGGGACGATATCGTCggggggG	ODN 2245	SEQ ID NO:9
	ggGGGACGACGTCGTCggggggG	ODN 2246	SEQ ID NO:10
	ggGGGACGAGCTCGTCggggggG	ODN 2247	SEQ ID NO:11
15	ggGGGACGTACGTCggggggG	ODN 2248	SEQ ID NO:12
	ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
	ggGGAACGATCGTCggggggG	ODN 2253	SEQ ID NO:14
	ggGGGACGATCGTCggggggG	ODN 2254	SEQ ID NO:15
	ggGGGACGATCGTCGggggggG	ODN 2255	SEQ ID NO:16
20	ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17
	ggGGTCGTCGACGAgggggG	ODN 2293	SEQ ID NO:18
	ggGGTCGTTTGAACGAgggggG	ODN 2294	SEQ ID NO:19
	ggGGACGTTTGAACGTggggggG	ODN 2295	SEQ ID NO:20
	ggGGAACGACGTCGTTggggggG	ODN 2297	SEQ ID NO:21
25	ggGGAACGTACGTCggggggG	ODN 2298	SEQ ID NO:22
	ggGGAACGTACGTACGTTggggggG	ODN 2299	SEQ ID NO:23
	ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
	ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
	ggGGACCGGTACCGGTggggggG	ODN 2302	SEQ ID NO:26
30	ggGTCGACGTCGAgggggG	ODN 2303	SEQ ID NO:27
	ggGGTCGACGTCGAgggg	ODN 2304	SEQ ID NO:28
	ggGGAACGTTAACGTTggggggG	ODN 2305	SEQ ID NO:29
	ggGGACGTCGACGTgggggG	ODN 2306	SEQ ID NO:30
	ggGGGTCGTTTCGTTggggggG	ODN 2311	SEQ ID NO:31
35	ggGACGATCGTCGggggggG	ODN 2328	SEQ ID NO:32
	ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
	ggTCGTCGACGAGggggggG	ODN 2330	SEQ ID NO:34
	ggGGACGATCGTCGggggggG	ODN 2332	SEQ ID NO:35
	ggGGTCGACGTCGACGTCGAGggggggG	ODN 2334	SEQ ID NO:36, and
40	ggGGACGACGTCGTGggggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

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8B7 176. A method of stimulating production of a plurality of type I IFN subtypes, comprising contacting IPCs with an amount of immunostimulatory nucleic acid effective to induce secretion of at least two type I interferons.

5 177. The method of claim 176, wherein the contacting occurs in vivo.

178. The method of claim 176, wherein the contacting occurs in vitro.

10 179. The method of claim 176, wherein the IPCs are precursor type 2 dendritic cells (pDC2s).

180. The method of claim 176, wherein the IPCs are isolated.

15 181. The method of claim 176, wherein the IPCs are induced to secrete at least three type I interferons.

182. The method of claim 176, wherein the IPCs are induced to secrete at least four type I interferons.

20 183. The method of claim 176, wherein the IPCs are induced to secrete at least five type I interferons.

184. The method of claim 176, wherein the IPCs are induced to secrete at least six type I interferons.

25 185. The method of claim 176, wherein the IPCs are induced to secrete at least seven type I interferons.

30 186. The method of claim 176, wherein the IPCs are induced to secrete at least eight type I interferons.

187. The method of claim 176, wherein the immunostimulatory nucleic acid is modified.

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188. The method of claim 176, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

189. The method of claim 176, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

190. The method of claim 176, wherein the immunostimulatory nucleic acid is not a palindrome.

191. The method of claim 176, wherein the immunostimulatory nucleic acid is a CpG nucleic acid.

192. The method of claim 176, wherein the immunostimulatory nucleic acid is a non-CpG nucleic acid.

193. The method of claim 192, wherein the non-CpG immunostimulatory nucleic acid is a T-rich nucleic acid.

194. The method of claim 192, wherein the non-CpG immunostimulatory nucleic acid is a poly-G nucleic acid.

195. The method of claim 176, wherein the immunostimulatory nucleic acid is any combination of at least two nucleic acids selected from the group consisting of: CpG nucleic acids, T-rich nucleic acids, and poly-G nucleic acids.

196. The method of claim 176, wherein the immunostimulatory nucleic acid is between 8 and 100 nucleotides in length.

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197. The method of claim 176, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

198. The method of claim 176, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

5	ggGGTCAACGTTGAgggggG	ODN 1585	SEQ ID NO:1
	tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
	ggggtcgtcgttttggggg	ODN 2184	SEQ ID NO:3
	tcgtcgttttgcgttttggggg	ODN 2185	SEQ ID NO:4
10	ggggtcgacgtcgaggggg	ODN 2192	SEQ ID NO:5
	ggggtcacgtcgaggggg	ODN 2204	SEQ ID NO:6
	ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
	gggggtcgtacgacggggg	ODN 2217	SEQ ID NO:8
	ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
15	ggGGGACGACGTCGTCgggggG	ODN 2246	SEQ ID NO:10
	ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
	ggGGGACGTACGTCgggggG	ODN 2248	SEQ ID NO:12
	ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
	ggGGAACGATCGTCgggggG	ODN 2253	SEQ ID NO:14
20	ggGGGGACGATCGTCgggggG	ODN 2254	SEQ ID NO:15
	ggGGGACGATCGTCGgggggG	ODN 2255	SEQ ID NO:16
	ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17
	ggGGTCGTCGACGAgggggG	ODN 2293	SEQ ID NO:18
	ggGGTCGTTTCAACGAgggggG	ODN 2294	SEQ ID NO:19
25	ggGGACGTTTCAACGTgggggG	ODN 2295	SEQ ID NO:20
	ggGGAACGACGTCGTTgggggG	ODN 2297	SEQ ID NO:21
	ggGGAACGTACGTCgggggG	ODN 2298	SEQ ID NO:22
	ggGGAACGTACGTACGTTgggggG	ODN 2299	SEQ ID NO:23
	ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
30	ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
	ggGGACCGGTACCGGTgggggG	ODN 2302	SEQ ID NO:26
	ggGTCGACGTCGAgggggG	ODN 2303	SEQ ID NO:27
	ggGGTCGACGTCGAgggg	ODN 2304	SEQ ID NO:28
	ggGGAACGTTAACGTTgggggG	ODN 2305	SEQ ID NO:29
35	ggGGACGTCGACGTgggggG	ODN 2306	SEQ ID NO:30
	ggGGGTCGTTTCGTTgggggG	ODN 2311	SEQ ID NO:31
	ggGACGATCGTCGgggggG	ODN 2328	SEQ ID NO:32
	ggGTCGTCGACGAggggggG	ODN 2329	SEQ ID NO:33
	ggTCGTCGACGAggggggG	ODN 2330	SEQ ID NO:34
40	ggGGACGATCGTCGgggggG	ODN 2332	SEQ ID NO:35
	ggGGTCGACGTCGACGTCGAgggggG	ODN 2334	SEQ ID NO:36, and
	ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

199. A method of inhibiting IL-12 production, comprising
contacting IL-12-producing cells, in the presence of interferon-producing cells under
conditions in which the IL-12-producing cells normally produce IL-12, with an
immunostimulatory nucleic acid in an amount effective for inducing secretion of type I
interferon.

200. The method of claim 199, wherein the immunostimulatory nucleic acid has a
sequence selected from the group consisting of

10	ggGGTCAACGTTGAggggggG	ODN 1585	SEQ ID NO:1
	tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
	ggggtcgtcgttttgggggg	ODN 2184	SEQ ID NO:3
	tcgtcgttttgcgttttgggggg	ODN 2185	SEQ ID NO:4
	ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
15	ggggtcacgtcgagggggg	ODN 2204	SEQ ID NO:6
	ggGGGACGATCGTCggggggG	ODN 2216	SEQ ID NO:7
	gggggtcgtacgacgggggg	ODN 2217	SEQ ID NO:8
	ggGGGACGATATCGTCggggggG	ODN 2245	SEQ ID NO:9
	ggGGGACGACGTCGTCggggggG	ODN 2246	SEQ ID NO:10
20	ggGGGACGAGCTCGTCggggggG	ODN 2247	SEQ ID NO:11
	ggGGGACGTACGTCggggggG	ODN 2248	SEQ ID NO:12
	ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
	ggGGAACGATCGTCggggggG	ODN 2253	SEQ ID NO:14
	ggGGGACGATCGTCggggggG	ODN 2254	SEQ ID NO:15
25	ggGGGACGATCGTCggggggG	ODN 2255	SEQ ID NO:16
	ggGGGTCATCGATGAggggggG	ODN 2260	SEQ ID NO:17
	ggGGTCGTCGACGAggggggG	ODN 2293	SEQ ID NO:18
	ggGGTCGTTTCAACGAggggggG	ODN 2294	SEQ ID NO:19
	ggGGACGTTTCAACGTggggggG	ODN 2295	SEQ ID NO:20
30	ggGGAACGACGTCGTTggggggG	ODN 2297	SEQ ID NO:21
	ggGGAACGTACGTCggggggG	ODN 2298	SEQ ID NO:22
	ggGGAACGTACGTACGTTggggggG	ODN 2299	SEQ ID NO:23
	ggGGTCACCGGTGAggggggG	ODN 2300	SEQ ID NO:24
	ggGGTCGACGTACGTCGAggggggG	ODN 2301	SEQ ID NO:25
35	ggGGACCGGTACCGGTggggggG	ODN 2302	SEQ ID NO:26
	ggGTCGACGTGAggggggG	ODN 2303	SEQ ID NO:27
	ggGGTCGACGTGAgggggg	ODN 2304	SEQ ID NO:28
	ggGGAACGTTAACGTTggggggG	ODN 2305	SEQ ID NO:29
	ggGGACGTCGACGTggggggG	ODN 2306	SEQ ID NO:30
40	ggGGGTCGTTTCGTTggggggG	ODN 2311	SEQ ID NO:31
	ggGACGATCGTCGggggggG	ODN 2328	SEQ ID NO:32
	ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
	ggTCGTCGACGAGggggggG	ODN 2330	SEQ ID NO:34
	ggGGACGATCGTCGggggggG	ODN 2332	SEQ ID NO:35

ggGGTCGACGTCGACGTCGAGgggggG ODN 2334 SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG ODN 2336 SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

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201. An isolated nucleic acid having a sequence selected from the group consisting of:

tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
ggggtcgtcgttttgggggg	ODN 2184	SEQ ID NO:3
tcgtcgttttgcgttttgggggg	ODN 2185	SEQ ID NO:4
10 ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
ggggtcatcgatgagggggg	ODN 2204	SEQ ID NO:6
ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
gggggtcgtacgacgggggg	ODN 2217	SEQ ID NO:8
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
15 ggGGGACGACGTCGTCgggggG	ODN 2246	SEQ ID NO:10
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGTACGTCgggggG	ODN 2248	SEQ ID NO:12
ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
ggGGAACGATCGTCgggggG	ODN 2253	SEQ ID NO:14
20 ggGGGACGATCGTCgggggG	ODN 2254	SEQ ID NO:15
ggGGGACGATCGTCgggggG	ODN 2255	SEQ ID NO:16
ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17
ggGGTCGTCGACGAgggggG	ODN 2293	SEQ ID NO:18
ggGGTCGTTTCAACGAgggggG	ODN 2294	SEQ ID NO:19
25 ggGGACGTTTCAACGTgggggG	ODN 2295	SEQ ID NO:20
ggGGAACGACGTCGTTgggggG	ODN 2297	SEQ ID NO:21
ggGGAACGTACGTCgggggG	ODN 2298	SEQ ID NO:22
ggGGAACGTACGTACGTTgggggG	ODN 2299	SEQ ID NO:23
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
30 ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACCGGTACCGGTgggggG	ODN 2302	SEQ ID NO:26
ggGTCGACGTCGAgggggG	ODN 2303	SEQ ID NO:27
ggGGTCGACGTCGAgggg	ODN 2304	SEQ ID NO:28
ggGGAACGTAAACGTTgggggG	ODN 2305	SEQ ID NO:29
35 ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGGGTCGTTCTGTTgggggG	ODN 2311	SEQ ID NO:31
ggGACGATCGTCGgggggG	ODN 2328	SEQ ID NO:32
ggGTCGTCGACGAggggggG	ODN 2329	SEQ ID NO:33
ggTCGTCGACGAGgggggG	ODN 2330	SEQ ID NO:34
40 ggGGACGATCGTCGgggggG	ODN 2332	SEQ ID NO:35
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

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202. A pharmaceutical composition comprising
an isolated nucleic acid having a sequence selected from the group consisting of:

	tcgtcgttttgcgttttgcgtt	ODN 2022	SEQ ID NO:2
5	ggggtcgtcgttttgggggg	ODN 2184	SEQ ID NO:3
	tcgtcgttttgcgttttgggggg	ODN 2185	SEQ ID NO:4
	ggggtcgacgtcgagggggg	ODN 2192	SEQ ID NO:5
	ggggtcacgtcgagggggg	ODN 2204	SEQ ID NO:6
	ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
10	gggggtcgtacgacgggggg	ODN 2217	SEQ ID NO:8
	ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
	ggGGGACGACGTCGTCgggggG	ODN 2246	SEQ ID NO:10
	ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
	ggGGGACGTACGTCgggggG	ODN 2248	SEQ ID NO:12
15	ggGGGACGATCGTTGggggG	ODN 2252	SEQ ID NO:13
	ggGGAACGATCGTCgggggG	ODN 2253	SEQ ID NO:14
	ggGGGACGATCGTCgggggG	ODN 2254	SEQ ID NO:15
	ggGGGACGATCGTCGgggggG	ODN 2255	SEQ ID NO:16
	ggGGGTCATCGATGAgggggG	ODN 2260	SEQ ID NO:17
20	ggGGTCGTCGACGAgggggG	ODN 2293	SEQ ID NO:18
	ggGGTCGTTCTGAACGAgggggG	ODN 2294	SEQ ID NO:19
	ggGGACGTTCTGAACGTgggggG	ODN 2295	SEQ ID NO:20
	ggGGAACGACGTCGTTgggggG	ODN 2297	SEQ ID NO:21
	ggGGAACGTACGTCgggggG	ODN 2298	SEQ ID NO:22
25	ggGGAACGTACGTACGTTgggggG	ODN 2299	SEQ ID NO:23
	ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
	ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
	ggGGACCGGTACCGGTgggggG	ODN 2302	SEQ ID NO:26
	ggGTCGACGTCGAgggggG	ODN 2303	SEQ ID NO:27
30	ggGGTCGACGTCGagggg	ODN 2304	SEQ ID NO:28
	ggGGAACGTTAACGTTgggggG	ODN 2305	SEQ ID NO:29
	ggGGACGTCGACGTgggggG	ODN 2306	SEQ ID NO:30
	ggGGGTCGTTCTGTTgggggG	ODN 2311	SEQ ID NO:31
	ggGACGATCGTCGgggggG	ODN 2328	SEQ ID NO:32
35	ggGTCGTCGACGAggggggG	ODN 2329	SEQ ID NO:33
	ggTCGTCGACGAGgggggG	ODN 2330	SEQ ID NO:34
	ggGGACGATCGTCGgggggG	ODN 2332	SEQ ID NO:35
	ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
	ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

40 wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage; and
a pharmaceutically acceptable carrier.

203. The pharmaceutical composition of claim 202, further comprising IFN- α .